Dockets Management Branch
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

December 31, 2003

Citizen Petition

Dear Sir or Madam:

The undersigned submits this petition under 21 CFR 10.25 and 10.30. This petition request that the Commissioner (1) review the safety of Nutropin Depot (Somatropin {rDNA orgin}Injection. Manufactured by Genentech Inc. Application No: 21-075, Approval Date: 12/22/00. (2) Issue direction to Genentench Inc. to add warnings regarding diabetes in their safety literature. (3) Consider amending 21 CFR 314.80(e) Postmarketing studies.

A. Action Requested

1. That the FDA's Adverse Event Reporting System (AERS), and more importantly, Genentech's National Cooperative Growth Study (NCGS) databases be reviewed for reported instances of diabetes and other serious adverse experiences, occurring during the use of Nutropin Depot or any of their other growth hormone products.

2. To require Genentech to include warning information in their "Your Family Guide To Preparing and Administering" and their "Important Safety Information" guides: about the symptoms of diabetes that parents should look for during the administration of growth hormone and that if the cell responsible for diabetes is present in the child, that it can trigger diabetes.

3. To consider amending 21 CFR 314.80(e) Postmarketing studies. Which presently reads: (1) An applicant is not required to submit a 15-day Alert report under paragraph (c) of this section for an adverse drug experience obtained from a postmarketing study (whether or not conducted under an investigational new drug application) unless the applicant concludes that there is a reasonable possibility that the drug caused the adverse event.

Change to read: (1) **An applicant is required to submit a 15-day Alert report under paragraph (c) for any serious adverse event reported to the applicant.** (2) An applicant is not required to submit a 15-day Alert report under paragraph (c) of this section for any adverse event (excepting (1) of this paragraph) obtained from a postmarketing study (whether or not conducted under an investigational new drug application) unless the applicant concludes that there is a reasonable possibility that the drug caused the adverse experience.

B. Statement of Grounds

Before setting forth the statement of grounds, I would like to introduce myself and the events which led to the need for this citizen petition. My name is[ ] In February 1998, my daughter [ ], was diagnosed with Turner Syndrome. One month later, in March of 1998, she was placed on Genentech's growth hormone Nutropin AQ. (a dosage of which had been found safe and effective through clinical studies of girls with Turner Syndrome). About three (3) years later, in October of 2000, she was placed on Genentech's growth hormone Nutropn Depot. The reason for the switch, was the convenience of two monthly injections, as opposed to daily. Within 28 days and a total of three (3) injections later, she was admitted to the emergency room, diagnosed with insulin-dependent diabetes mellitus.

I had never heard of Turner Syndrome, and so far as diabetes was concerned, I believed it was something one got from eating too many sweets. An important point to remember is that, the majority of

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parents, having no basis of understanding of diseases, rely predominantly upon the information the doctor presents to them as being unabridged, truthful and accurate.

1. I have enclosed the AERS report for Nutropin Depot from Nov 1997 through Apr 2003. {Attachment #1} It differs in the number of insulin-dependent diabetes mellitus (IDDM) for girls with Turner Syndrome administered Nutropin Depot. Dr Wagner (Genentech) reported one (1) from the National Cooperative Growth Study (NCGS) database. The number reported by the FDA's Adverse Event Reporting System (AERS) database was two (2). Seeking to identify the true numbers, I requested the help of my daughters doctor. He stated there was a registry he could get this information from. He however, never initially identified the registry as the NCGS funded by Genentech. I have enclosed e-mails between my daughters doctor, myself and the responses from Genentech.{Attachment #2 - 5)

My daughters doctor initially reported to Genentech (in his investigative report) that the event was 'unlikely' related to the drug. Here again, he states he reported it to a registry, but doesn't identify the registry as Genentech (NCGS) registry. I believed he was referring to the FDA. He further never identified the fact that he was an investigator for Genentechs growth hormone products and that he had known the executives for over 20 years. He related to me, that his conclusion for choosing 'unlikely' related, was based on the fact that the incidence of IDDM in growth hormone treated children has been watched since 1984. And that there is no reported evidence of an increased incidence. What significance, does what he had said, have? He is not reporting it as 'possibly' because nobody else has. However, in my daughters Discharge Summary (Attachment #6), he does note that the diabetic symptoms occurred within the time frame of starting the Nutropin Depot.

Herein lies the problem. Once he had indicated in his report (imputed into the NCGS database) his conclusion, that it was 'unlikely' related to the event, it provided a "free pass " to Genentech. Genentech, was now under no obligation to report the event to the FDA, and they did not, until March 7, 2003 when my daughters doctor directed his conclusion be changed from 'unlikely' to 'possibly'. This now mandated , that what had previously been an unreported serious adverse event, was now reported into the FDA AERS database.(Attachment #7). What prompted this change in his conclusion? Could it be the possible dangers it presents to girls with Turner Syndrome, or perhaps the more I learned and relayed to him I knew, the more he was inclined to admit. Finally, he never reported the event to FDA via MedWatch, even after I had personally requested that he do so.

How many other similar scenarios, are being played out each day between doctor, patient and uninformed parents? The truth lies in the NCGS database. (Attachment# 8). The information imputed into the databases of the manufactures of growth hormone, must be requested and evaluated, to insure the safety of the children considering using growth hormone. Presently, the only documented and published information on Nutropin Depot are the results of clinical trials. **No one, including the FDA, (with the exception of Genentech) was aware of my daughters serious adverse event.** Genentech knew of my daughters onset immediately following the event. How many other cases is Genentech aware of, that the FDA is not aware of?

2. Eli Lilly and Co, in their safety information regarding pediatric patients indicates under: What condit.ons should I be aware of while my child is receiving Humatrope? Growth hormone affects the body's glucose metabolism. If your child develops symptoms such as increased urination or thirst, notify you child's doctor as these may be symptoms of diabetes or glucose intolerance. What is it that prompted Eli Lilly and Co to include this warning? What has been reported to their safety division (that has not been reported to the FDA) and how often has it been reported, reflecting the symptoms of diabetes? What is in their database? (Attachment #9)

Serono Co, in their safety information regarding pediatric patients indicates in their: How Kids Grow, A Parent's Guide: under Physical Effects of Growth Hormone Treatment: If a child's family has a history of insulin-independent diabetes mellitus (high blood sugar), growth hormone treatment may trigger that disease. What is it that prompted Serono Co to include this warning? What has been reported to their safety division (that has not been reported to the FDA) and how often has it been reported, reflecting the onset of insulin-dependent diabetes mellitus during growth hormone treatment? What is in their database?

(Attachment #10)

Genentech Inc., does not give mention to either of the above indicated warnings (as Eli Lilly and Serono do) in either their Important Safety Information or in their: Your Family's Guide To Preparing and Administering. (Attachment #11 & #12) After my daughters 2nd injections of Nutropin Depot, she was showing the signs and symptoms of diabetes. Had the warning of the symptoms been in Genentechs guide, I would have immediately notified my daughters doctor of her status. As it was at the time, I believed the increased hunger, thirst and urination to be the result of the increased amount of growth hormone injected in the Deport preparation. (Five times that of a daily injection). Had the warning that growth hormone could trigger type 1 diabetes in a child who has the cell responsible for type 1 diabetes in their cellular makeup, I would have never agreed to place my child at risk (due to her Turner Syndrome) for mere cosmetic reasons gaining a few inches in height..

3. The FDA has no regulatory authority over the practice of medicine. Only a state board of medicine has such authority. This results in a situation, in which mandates, regulations or policies cannot be initiated with regard to doctors. However, I believe the amending of 21 CFR 314.80(e) will provide the avenue necessary, for information reported to manufactures by doctors administering new drugs which result in serious adverse events, to be timely transmitted to the FDA. Only then can the FDA make accurate and reasonable determination as to the drugs safety. This in turn, will allow for the documentation and publication of events resulting in serious adverse experiences, to which the medical community will be aware of and not working in an environment of uniformed possibilities. I have on a personal level, advanced the idea of legislating new requirements for doctors to report the occurrences of serious adverse events to the FDA via MedWatch in my state. (Attachment #13). If successful , this will only be applicable to my state. The amending of 21CFR 314.80(e) will encompass all manufacturers of new drugs. Not perfect, but far and above what is presently the state of accountability and responsibility the exists .

C. Environmental Impact

An environmental assessment on the action requested in this petition qualifies for a categorical exclusion under 21 CFR 25.30 Therefore, an environmental assessment is not required for the requested action.

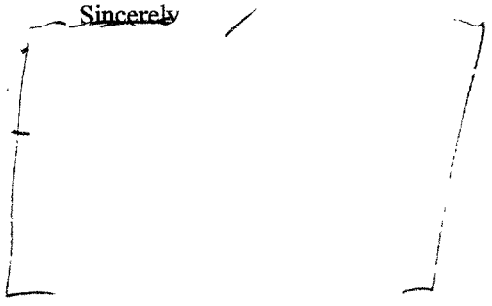
D. Economic Impact

Pursuant to 21 CFR 10.30, economic impact information is to be submitted only when requested by the Commissioner. This information will be promptly provided, if so requested.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and the includes representative data and information known to the petitioner, which are unfavorable to the petition.

Sincerely



Attachments

1. Adverse Event Reporting System (AERS) for Nutropin Depot
   From: 01-NOV-1997 TO 28-APR-2003
2. Electronic mail regarding: NCGS Database Information
3. Electronic mail regarding: NCGS Database Information
4. Electronic mail regarding: NCGS Database Information
5. Electronic mail regarding: NCGS Database Information
6. Hospital Discharge Summary
7. Electronic mail regarding: 21 CFR 314.80(C)(2)(e) Postmarketing studies
8. National Cooperative Growth Study NCGS Description of Functions
9. Eli Lilly - Warning regarding diabetes
10. Serono - Warning regarding diabetes
11. Genentech's Important Safety Information (No warnings regarding diabetes)
12. Genentech's Your Family's Guide To Preparing And Administering Nutropin Depot (No warnings regarding diabetes)
13. Electronic mail regarding: Reporting of Serious Adverse Events by Doctors to FDA through State Legislation